

REMARKS/ARGUMENTS

Claims 8, 10, 11, 13, 14, 16, 17 and 19 are currently pending in the application. The Examiner has withdrawn claims 8 and 10 from consideration. It is understood that withdrawn method claims will be rejoined upon allowance of a product claim. Such rejoinder is respectfully requested. Applicants have canceled claims 9, 12, 15, 18 and 20 herein. Applicants reserve the right to pursue the subject matter of these claims in a continuation application. Applicants have amended claims 8, 10, 11, 13, 14, and 16. Support for the amendments to claims 8, 11 and 14 can be found at page 6, lines 12-15 (a preparation of at least 70% mesenchymal stem cells). Claims 10, 13 and 16 have been amended to delete trademarks. No new matter has been added.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 12, 13, 15, 16, 18 and 19 under 35 U.S.C. § 112, second paragraph for indefiniteness. The Examiner argued that the claims disclosed the trademarks Ficoll® or Percoll® and that these trademarks rendered the claims indefinite. Applicants have canceled claims 12, 15 and 18 rendering this rejection moot as it applies to these claims.

Applicants respectfully disagree, but to facilitate prosecution, have amended claims 13 and 16 to delete reference to Percoll®. Applicants submit that claim 19 does not recite trademarks. Thus, Applicants assert that claims 13, 16 and 19 are definite and respectfully request that this rejection be withdrawn.

Rejections under 35 U.S.C. § 102/103

The Examiner rejected claims 11-19 under 35 U.S.C. § 102(b) or in the alternative, 35 U.S.C. § 103 for being anticipated or obvious over the teachings of Thiede *et al.*, U.S. Patent No. 5,965,436 ("Thiede"). The Examiner argued that because claims 11-19 are product by process claims, that the structure implied by the process steps should be considered when assessing the patentability of a product by process claim. The Examiner further argued that the USPTO is not equipped to conduct experimentation in order to determine whether or not Applicants' mesenchymal stem cells (MSCs) differ from the MSCs described in Thiede. The Examiner requested clear evidence that the MSCs in Thiede do not possess a critical characteristic of the MSCs of claims 11-19. Applicants have canceled claims 12, 15 and 18 rendering this rejection moot as it applies to these claims. Applicants respectfully traverse.

Applicants submit that Thiede cannot anticipate claims 11, 13, 14, 16, 17 and 19.

Applicants have amended claims 11 and 14, from which claims 13, 16, 17 and 19 depend, to state the fraction from which the MSCs are isolated must contain more than 70% human MSCs. Thiede teaches the isolation of mesenchymal stem cells associated by isolating megakaryocytes with which the MSCs are associated.¹ Thiede teaches that the ratio of megakaryocyte to MSC is much higher than 1:1, as shown in Figures 1 and 2. Thus, the fractions shown in Thiede must contain at least 50% megakaryocytes. Claims 11, 13, 14, 16, 17 and 19 specify that the fraction from which the human MSCs are isolated must contain at least 70% MSCs. Thiede does not teach this limitation.

Moreover, Thiede only teaches the isolation of MSCs with megakaryocytes in human tissue in a fraction at a density of 1.073 g/ml.² Isolation of MSCs with megakaryocytes in fractions at lower densities is only shown with canine cells. For example, the results for densities shown in the table in column 4 of Thiede and also described in Figure 4 are from canine cells as shown at the brief description of Figure 4.³ The same cells were used in Figures 5 and 6. Human cells are only shown in Figures 7-9, which were isolated from the 1.073 g/ml fraction.⁴

Thiede does not teach each and every limitation of claims 11, 13, 14, 16, 17 and 19. Thus, Applicants submit that Thiede cannot anticipate the claims and respectfully request that this rejection be withdrawn.

Applicants further submit that claims 11, 13, 14, 16, 17 and 19 are not obvious over the teachings of Thiede. Applicants argue that the Examiner has not provided a proper *prima facie* case of obviousness. Further, Applicants argue that Thiede teaches away from the invention of 11, 13, 14, 16, 17 and 19. Moreover, Applicants argue that the instant specification shows evidence of unexpected results which the Examiner has not considered.

No Prima Facie Case of Obviousness

Applicants assert that the Examiner has not provided a *prima facie* case of obviousness of claims 11, 13, 14, 16, 17 and 19 over the teachings of Thiede. Prior art is not limited just to the

¹ See Thiede at the Title.

² *Id.* from column 6, line 54 to column 8, line 30.

³ *Id.* at column 2, lines 13-17.

⁴ *Id.* at column 8, lines 1-30.

references being applied, but includes the understanding of one of ordinary skill in the art. The prior art reference (or references when combined) need not teach or suggest all the claim limitations, however, Office personnel must explain why the difference(s) between the prior art and the claimed invention would have been obvious to one of ordinary skill in the art.⁵ As explained above, Thiede does not teach or suggest the limitations of claims 11, 13, 14, 16, 17 and 19 and the Examiner has not explained why the differences would be obvious to one of ordinary skill in the art. Thus, the Examiner has not shown a *prima facie* case of obviousness.

Teaching Away

Moreover, Thiede teaches away from the invention of claims 11, 13, 14, 16, 17 and 19. A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. In re Gurley, 27 F.3d 551, 553 (Fed. Cir. 1994). Thiede teaches the isolation of MSCs based on their association with megakaryocytes. Thiede first teaches using a density gradient fraction with a higher density than the range of claims 11, 13, 14, 16, 17 and 19. Thiede also does not teach that this fraction will have at least 70% human MSCs. Thiede also teaches that a subsequent step is necessary to isolate MSCs from the megakaryocytes. For example, CD41 antibodies are used to isolate human MSCs away from megakaryocytes.⁶ This step is unnecessary in the invention of claims 11, 13, 14, 16, 17 and 19. The teachings of Thiede would send a person of ordinary skill on a path divergent from the one taken by the Applicants and thus teaches away from the invention of claims 11, 13, 14, 16, 17 and 19.

Secondary Considerations

The Applicants submit that there are secondary considerations present here that evidence the non-obviousness of the claimed invention. The USPTO must give secondary considerations due weight. See In re Sernaker, 702 F.2d 989 (Fed.Cir. 1983).

One secondary consideration that is present here is surprising or unexpected results. The specification teaches that human MSCs isolated from a fraction of a density within the range of

⁵ MPEP § 2141

⁶ Id. at column 7, lines 40-58.

claims 11, 13, 14, 16, 17 and 19 have enhanced capacity for proliferation.⁷ Human MSCs isolated from fractions with densities 1.05 to 1.068 g/ml achieve more cell divisions than cells isolated from higher densities.⁸ Moreover, human MSCs isolated from isolated from fractions with densities 1.05 to 1.068 g/ml have more colony forming unit-fibroblasts (CFU-f) than those from heavier fractions.⁹ Also, cells from the heavier fractions showed a reduction in CD90 and CD105 positive cells.¹⁰ CD90 is a marker for early progenitor cells and CD105 is an MSC specific marker.¹¹

Based on the above evidence, the superior properties of human MSCs isolated from fractions with densities 1.05 to 1.068 g/ml would not have been expected based on the teachings of Thiede.

For the above reasons, Applicants submit that claims 11, 13, 14, 16, 17 and 19 are non-obvious over the teachings of Thiede and respectfully requests that this rejection be withdrawn.

⁷ See the specification at page 6, lines 3-8.

⁸ *Id.* at page 16, lines 1-4 and Figures 2 and 3.

⁹ *Id.* at page 16, lines 11-16 and Figure 4.

¹⁰ *Id.* at page 17, lines 6-14.

¹¹ *Id.* at page 16, lines 17-20.

CONCLUSION

Applicants respectfully request prompt examination in the application. If there are any questions regarding this Response, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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